U.S. Food and Drug Administration

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Summary Minutes of the
Advisory Committee for Reproductive Health Drugs
June 18, 2010

Location: Hilton Washington DC North/Gaithersburg, 620 Perry Parkway, Gaithersburg, Maryland

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the June 18, 2010 Meeting of the Advisory Committee for Reproductive Health Drugs of the Food and Drug Administration were approved on August 24, 2010.

I certify that I attended the June 18, 2010, Meeting of the Advisory Committee for Reproductive Health Drugs of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____
Kalyani Bhatt
Designated Federal Official, ACHRD

_____/s/_____
Julia V. Johnson, M.D.
Committee Chair

The Advisory Committee for Reproductive Health Drugs of the Center for Drug Evaluation and Research met on June 18, 2010 at the Hilton Washington DC North/Gaithersburg, The Ballrooms, 620 Perry Parkway, Gaithersburg, Maryland. Prior to the meeting, members and invited consultants were provided background material from the FDA and Sponsor. The meeting was called to order by Julia V. Johnson, M.D., Acting Chair; the conflict of interest statement was read into the record by Kalyani Bhatt (Designated Federal Official). There were approximately two hundred (200) persons in attendance. There were twelve (12) speakers for the Open Public Hearing Session.

Issue: New drug application (NDA) 22-526, (flibanserin) tablets, 100 milligrams (mg), Boehringer Ingelheim Pharmaceuticals, Inc., for the proposed indication of the treatment of hypoactive sexual desire disorder (HSDD) in premenopausal women.

Attendance:

Advisory Committee for Reproductive Health Drugs Members (Voting):
Julia V. Johnson, M.D. (Acting Chair), Kathleen Hoeger, M.D., M.P.H., John Kittelson, Ph.D., Valerie Montgomery Rice, M.D.

Industry Representative Member (Non-Voting): Industry Representative was not present at the meeting.

Patient Representative: Patient Representative was not present at the meeting.

Special Government Employee Consultants (Temporary Voting Members):
Diane Aronson (Acting Consumer Representative**);** Marianne Brandon, Ph.D., Scott Emerson, M.D., Ph.D., Julia R. Heiman, Ph.D., Paula Hillard, M.D., Bryce B. Reeve, Ph.D., Matthew V. Rudorfer, M.D.

FDA Participants (Non-Voting): Julie Beitz, M.D., Scott Monroe, M.D., Lisa Soule, M.D., Dan Davis, M.D., Olivia Easley, M.D., LaiMing Lee, Ph.D., Lisa Kammerman, Ph.D.

Advisory Committee for Reproductive Health Drugs Members Not Present: Sandra Carson, M.D., Paul Blumenthal, M.D., M.P.H., Richard Bockman, M.D., Maria Bustillo, M.D., Bart Clarke, M.D., Daniel L. Gillen, Ph.D., Melissa Gilliam, M.D., Robert Gut, M.D., Ph.D., James H. Liu, M.D.

Designated Federal Official: Kalyani Bhatt, B.S., M.S.

Open Public Hearing Speakers:

1. Sue Goldstein
2. Irwin Goldstein, MD, Director, Sexual Medicine, Alvarado Hospital, San Diego, CA
   Clinical Professor of Surgery, University of California at San Diego
   Editor-in-Chief, The Journal of Sexual Medicine
3. Leonore Tiefer, PhD, Clinical Assoc. Professor
   Department of Psychiatry
   NYU School of Medicine
4. Dr. Thea Cacchioni ,Lecturer, Sociology
   Irving K. Barber School of Arts & Sciences
   University of British Columbia Okanagan
5. Michelle King Robson, Founder/CEO EmpowHER
6. Karen M. Hicks, Ph.D.
7. Susan Wysocki, The National Association of Nurse Practitioners in Women's Health (NPWH)
8. Adriane Fugh-Berman, MD, Associate Professor, Georgetown University Medical Center and Director of PharmedOut
   Elena Yanchar and Antonie Meixel
9. Liz Canner, Director
   Astrea Media, Inc.
10. Wayne C. Shields
    President and CEO, Association of Reproductive Health Professionals
11. Amy Allina, Program Director
    National Women's Health Network
12. Kim Whittemore

AGENDA

Call to Order and Introductions	Julia Johnson, M.D., Acting Chair Advisory Committee for Reproductive Health Drugs (ACRHD)
Conflict of Interest Statement ACRHD	Kalyani Bhatt, B.S., M.S. Designated Federal Official,
Welcome and Comments	Scott Monroe, M.D. Director, Division of Reproductive and Urologic Products (DRUP)
Sponsor Presentation	Boehringer Ingelheim Pharma., Inc. Sabine Luik, M.D. Corporate Senior Vice President Quality, Regulatory, Pharmacovigilance and Epidemiology Boehringer Ingelheim GmbH
	Anita Clayton, M.D David C. Wilson Professor of Psychiatry & Neurobehavioral Professor of Clinical Obstetrics & Gynecology University of Virginia
	Michael Sand, Ph.D., M.P.H. Global Strategic Leader, flibanserin Director, General Medicine Boehringer Ingelheim
Pharmaceuticals	
	Lutz Hilbrich, M.D. Executive Director, General
Medicine Pharmaceuticals	Boehringer Ingelheim
	Anita Clayton, M.D
FDA Presentation	

Efficacy	Daniel Davis, M.D. Medical Officer DRUP
Safety	Olivia Easley, M.D. Medical Officer DRUP
Clinical Pharmacology	LaiMing Lee, Ph.D. Clinical Pharmacologist Office of Clinical Pharmacology (OCP)

Questions from the Committee to Sponsor and FDA

Open Public Hearing

Committee Discussion and Voting
Adjournment

Questions to the Committee

1. Considering that the two primary US efficacy studies did not demonstrate efficacy for the prespecified co-primary endpoint of sexual desire as measured by the daily eDiary:
    a. Do you agree with the Applicant that the impact of flibanserin on sexual desire is better evaluated with the desire domain of the FSFI using 28-day recall?
    (Vote)

    Yes- 2 No - 9 Abstain- 0

    Overall, those that voted yes noted that the FSFI (Female Sexual Function Index) is a standardized tool and although imperfect, it is a standardized tool for looking at sexual desire.-The daily diary is not a verified tool, while the FSFI is a well-known and published tool where as the daily diary is a non-standardized tool.

    Overall, those that voted no recognized that the Sponsor and FDA had agreed a priori on the use of the eDiary. The group as a whole felt that some form of daily measurement is of greater value than the 28-day recall used by the FSFI. It was also mentioned that for future consideration utilizing the daily dairy and putting it into a monthly format may offer some valuable information.

    Please see the transcript for detailed discussion.

    b. Is it appropriate to alter the prespecified method of assessing sexual desire?
    (Vote)

    Yes- 2 No - 9 Abstain- 0

    Overall, those that voted yes stated that it was appropriate to alter the pre-specified method of assessing sexual desire from the eDiary (electronic diary) to the FSFI (Female Sexual Function Index) as they reasoned that the FSFI is a standardized and tested tool.

    Overall, those that voted no felt that altering the pre-specified method of assessing sexual desire during the clinical trial did not maintain the integrity of the trial. Those that voted no also felt that changing the method should have been addressed earlier than the Phase 3 trial.

    Please see the transcript for detailed discussion.

2. Has the Applicant provided sufficient evidence of overall efficacy for flibanserin for the treatment of hypoactive sexual desire disorder (HSDD) compared to placebo?
    (Vote)

    Yes- 1 No - 10 Abstain- 0

The committee's consensus was that the applicant did not provide sufficient evidence of the overall efficacy for flibanserin for the treatment of hypoactive sexual desire disorder (HSDD) as concerns were raised that improvement was not shown in sexual desire through the eDiary between flibanserin and placebo. It was recognized that there was a significant improvement in SSE between flibanserin and placebo, and patient satisfaction with the treatment was noted

The committee raised concerns regarding the number of individuals who dropped out due to adverse events. Due to the high drop out rate and the design of the study for those who dropped out to consider themselves as being closed out of the study, the Committee did not feel that they had the necessary information to evaluate this medication effectively. During discussion, it was identified that HSDD is a real condition; however, the diagnosis is still challenging. The committee acknowledged that indeed there is a significant need for women to have a treatment for HSDD and that efforts need to be put forth to continue to find ways to treat this disorder.

Please see the transcript for detailed discussion.

3. Considering the available data on efficacy and safety, has the Applicant demonstrated that the overall risk/benefit profile of flibanserin for the treatment of HSDD in premenopausal women is acceptable?

   (Vote)

   Yes-0 No -11 Abstain-0

   The Committee felt that that the efficacy of flibanserin was not sufficiently robust to justify the risks. Overall, the Committee was concerned over the safety signals seen. Concerns were also raised regarding potential drug interactions with flibanserin. The Committee felt that data needed to be provided on the long term use of flibanserin. Further documentation of improved sexual desire is critical for reconsideration of this medication for treatment of HSDD.

Please see the transcript for detailed discussion.

The meeting adjourned at approximately 3:30 PM.